Attorney Docket No. ORT-1414

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

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Re: U.S. PATENT APPLICATION
Serial Number 09/833,222

Filed: April 11, 2001 Art Unit 1647

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DECLARATION OF DR. NING QI UNDER RULE 37 CFR 1.131

1. I am a co-inventor of the application Serial Number 09/833,222, entitled "cDNA Encoding the Human Alpha2Delta-4 Calcium Channel Subunit" (the '222 application). I obtained my Ph.D. degree in July 1993, from Baylor College of Medicine, and had my postdoctoral training at University of California, Los Angeles from 1994-1997. From 1997 to 1999, I was employed as a research assistant professor at UCLA and then, as an Assistant Professor at University of Kentucky. I have been employed by Johnson & Johnson as a research scientist since September 1999. My resume is attached as Exhibit 1.

2. The invention described in the '222 application is based on the research my colleague and I conducted from 1999 to 2000, during which we successfully cloned the human $\alpha_2\delta$-4 calcium channel subunit, as evidenced by the data in my laboratory notebook. I attach the relevant notebook pages (Exhibits 2 and 3) and a computer printout (Exhibit 4) herewith to demonstrate the process of our invention. This was completed long before the Brown and Bertelli's publication (March 22, 2001, WO 01/19870A2).

3. I was interested in cloning this subunit because the voltage gated calcium channel is one of important pain therapeutic targets as recognized by the scientists in the field of pain control. I believe that the $\alpha_2\delta$ is a key regulatory subunit and that there are multiple $\alpha_2\delta$ isoforms, based on our analysis on human genomic DNA data, all play an important role in mediating Ca^{2+} influx in excitable cells.

4. I started the project of cloning $\alpha_2\delta$–4 on or about September 20, 1999 (Exhibit 12. No. 15798-1) and my colleague and I continuously worked on the project for the next several months. Because the cDNA encoding $\alpha_2\delta$-4 subunit is more than 3Kb, I had to clone it piece by piece. (Exhibit 2). We ultimately assembled and sequenced the fully length cDNA of $\alpha_2\delta$-4 subunit by April 7, 2000, which was recorded in my lab notebook (Exhibit 3, p. No. 15798-139), and the DNA and protein sequence information were also documented in both Microsoft word and Seqweb files on the same day. (Exhibit 4).

I declare under the penalty of perjury that the above statements are true and accurate to the best of my knowledge.

Dated: June 6, 2006 By: _____
Ning Qin, Ph.D.

CURRICULUM VITAE

[04-30-2006]

Ning Qin

SITE: Spring House

DIVISION: Analgesics

DEPARTMENT: Drug Discovery

EDUCATION: Baylor College of Medicine, Houston, Texas
1993, Biochemistry, Ph.D.

EMPLOYMENT

1999-present Johnson & Johnson Pharmaceutical Research and Development
Spring House, PA
2003-Present Principal Scientist, Analgesics, Drug Discovery
1999-2002 Senior Scientist

1999- Department of Pharmacology, University of Kentucky
Lexington, KY 40536
1999-1999 Assistant Professor

1994-1998 Dept. of Anesthesiology UCLA. School of Medicine,
Los Angeles, CA 90095
1997-1998 Research Assistant Professor
1994-1996 Postdoctoral Fellow

CURRENT PROFESSIONAL AFFILIATIONS

1. Society of Neuroscience
2. Biophysical Society
3. American Pain Society
4. International Association for the study of Pain
5. New York Academy of Sciences

PUBLICATIONS

Manuscripts

1. **N. Qin,** S. J. Pittler and W. Baehr, (1992) "*In Vitro* Isoprenylation and Membrane Association of Mouse Photoreceptor cGMP Phosphodiesterase α and β subunits Expressed in Bacteria", ***Journal of Biological Chemistry,*** 267, 8458-63

2. **N. Qin** and W. Baehr, (1993) "Expression of Mouse Rod Photoreceptor PDE γ Subunit in Bacteria", ***FEBS Letters,*** 321, 6-10

3. M. L. Suber, S. J. Pittler, **N. Qin,** G. C. Wright, V. Holcombe, R. H. Lee, C. M. Craft, R. N. Lolley, W. Baehr and R. L. Hurwitz, (1993) "Irish Setter Dogs Affected with Rod/Cone Dysplasia Contain a Nonsense Mutation in the Rod cGMP Phosphodiesterase β Subunit Gene", ***Proc. Natl. Acad. Sci. U.S.A.*** 90, 3968-3972

4. **N. Qin** and W. Baehr, (1994) "Expression and Mutagenesis of Biologically Active Mouse Rod Photoreceptor cGMP Phosphodiesterase", ***Journal of Biological Chemistry,*** 269 3265-3271

5. T. Schneider, X. Wei, R. Olcese, J. L. Costantin, A. Neely, P. Palade, E. Peryes, **N. Qin,** J. Zhou, G. Crawford, R. G. Smith, S. H. Appel, E. Stefani and L. Birnbaumer (1994) "Molecular analysis and functional expression of the human type E neuronal Ca^{2+}-channel α_1 subunit", ***Receptors and Channels,*** 2, 255-270

6. R. Olcese, **N. Qin** ***(Co-first author),*** T. Schneider, A. Neely, X. Wei, E. Stefani and L. Birnbaumer (1994) "The Amino Terminus of a Calcium Channel β subunit Sets Rates of Channel Inactivation Independently of the Subunit's Effect on Activation", ***Neuron,*** 13, 1433-1438

7. F. Noceti, P. Baldelli, X. Wei, **N. Qin,** L. Toro, L. Birnbaumer and E. Stefani (1996) "Effective Gating Charges Per Channel in Voltage Dependent K^+ and Ca^{2+} Channels", ***J. Gen. Physiol.*** 108, 143-155

8. **N. Qin**, R. Olcese , J. Zhou O. Caballo, L. Birnbaumer and E. Stefani (1996) "Identification of a second region of the β subunit involved in regulation of calcium channel inactivation", ***Am. J. Physiol. (Cell Physiology),*** 271:C1539-C1545

9. R. Olcese, A. Neely, **N. Qin**, X. Wei, L. Birnbaumer and E. Stefani (1997) "Coupling Between Charge Movement and Pore Opening in Neuronal α_{1E} Calcium Channel." ***J. Physiol.*** 497, 675-686

10. E. Tareilus, M. Roux, **N. Qin,** R. Olcese, J. Zhou E. Stefani and L. Birnbaumer (1997) "A Functional Calcium channel β subunit is Expressed in *Xenopus* Oocytes", ***Proc. Natl. Acad. Sci. U.S.A.*** 94, 1703-1708

11. J. Zhou R. Olcese, **N. Qin**, E. Stefani and L. Birnbaumer, (1997) "Feedback inhibition of calcium channels by calcium depends on a short sequence of the carboxyterminus that does not include the Ca^{2+} binding function of a motif with similarity to calcium binding domains", ***Proc. Natl. Acad. Sci. U.S.A.*** 94, 2301-2305

12. **N. Qin**, D. Platano, R. Olcese, E. Stefani and L. Birnbaumer (1997) "Inhibition of Neuronal Ca^{2+}Channel G-protein Coupled receptors Mediated by a Small C-terminal Gβγ Binding Domain of α_1", ***Proc. Natl. Acad. Sci. U.S.A.*** 94, 8866-887.

13. J. Costantin, F. Noceti, **N. Qin,** X. Wei, L. Birnbaumer and E. Stefani, (1998) "Facilitation by the β Subunit of Pore Openings in Cardiac Ca^{2+} Channels", ***J. Physiol.*** 507, 93-103

14. F. Noceti, R. Olcese, **N. Qin,** and E. Stefani, (1998) "Ca^{2+}-dependent inactivation in α_{1C} Ca^{2+} channels: effect of Bay K 8644(-) and the β_{2a} subunit. A model", ***J. Gen. Physiol.*** 111, 463-475

15. **N. Qin**, R. Olcese, E. Stefani and L. Birnbaumer (1998) "Modulation of human neuronal α_{1E} type calcium channel by $\alpha_2\delta$ subunit", ***Am. J. Physiol. (Cell Physiology),*** 274, C1324-C1331

16. **N. Qin,** Platano, R. Olcese, J. Costantin, E. Stefani and L. Birnbaumer (1998) "Unique regulatory properties of type 2a Ca^{2+} channel β subunit due to palmitoylation", ***Proc. Natl. Acad. Sci. U.S.A***,95, 4690-4695

17. N. Li, R.N. Fariss, K. Zhang, A. Otto-Bruc, F. Haeseleer, D. Bronson, **N. Qin**, A. Yamazaki, I. Subbaraya, A. H. Milam, K. Palczewski and W. Baehr, (1998) "Guanylate-cyclase-inhibitory protein is a frog retina Ca^{2+} binding protein related to mammalian guanylate-cyclase-activating protein", **Eur. J. Biochem**. 252, 591-59

18. J. Costantin, **N. Qin,** L. Birnbaumer and E. Stefani, (1998) "Long lasting voltage-dependent facilitation of a cardiac and brain calcium channel: correlation with the coupling efficiency between charge movement and pore opening", **FEBS Letter,** 423, 213-217

19. M. Ottolia, D. Platano, **N. Qin** M. Birnbaumer, L. Toro, L. Birnbaumer, E. Stefani and R. Olcese (1998) "Functional Coupling Between Human E-type Ca^{2+} Channels and μ Opioid Receptors Expressed in *Xenopus* Oocytes"; **FEBS Letter,** 427, 96-102

20. J. Costantin, **N. Qin,** M. N. Waxham, L. Birnbaumer and E. Stefani, (1999) "Complete reversal of run-down in rabbit cardiac Ca2+ channels by patch-cramming in Xenopus oocytes; partial reversal by protein kinase A". **Pflugers Arch;** 437(6): 888-94

21. **N. Qin,** R. Olcese, M. Bransby, T. Lin, and L. Birnbaumer (1999) "Ca^{2+}-induced inhibition of the cardiac Ca^{2+} channel depends on calmodulin". ***Proc. Natl. Acad. Sci. U S A*;** 96(5): 2435-8

22. B. Vannier, M. Peyton, G. Boulay, D. Brown, **N. Qin,** M. Jiang, X. Zhu, and L. Birnbaumer (1999) "Mouse trp2, the homologue of the human trpc2 pseudogene, encodes mTrp2, a store depletion-activated capacitative Ca^{2+} entry channel" ***Proc. Natl. Acad. Sci. U S A*;** 96(5): 2060-4

23. G. Boulay, D. M. Brown, **N. Qin** ***(Co-first author)***, M. Jiang, A. Dietrich, M. X. Zhu, Z. Chen, M. Birnbaumer, K. Mikoshiba, and L. Birnbaumer (1999) "Modulation of Ca^{2+} entry by polypeptides of the inositol 1,4,5-trisphosphate receptor (IP3R) that bind transient receptor potential (TRP): Evidence for roles of TRP and IP3R in store depletion-activated Ca^{2+} entry" ***Proc. Natl. Acad. Sci. U S A***; 96: 14955-14960.

24. D. Platano, **N. Qin,** F. Noceti, L. Birnbaumer, E. Stefani, and R. Olcese (2000) "Expression of alpha2delta Subunit Interferes with Prepulse Facilitation in Cardiac L-type Calcium Channels" ***Biophys. J.*** 78 2959-2972

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26. **N. Qin**, S. Yagel, M. Momplaisir, E. E. Codd and M. R. D'Andrea (2002) "Molecular cloning and characterization of human voltage-gated calcium channel $\alpha_2\delta$-4 subunit" ***Molecular Pharmacology, 62 (3)***

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28. **N. Qin,** M. D'Andrea, M. Lubin, N. Shafaee, E. Codd and A. Correa (2003) "Cloning and Characterization of a novel splicing variant of human sodium channel β_1 subunit". ***The FEBS Journal (European Journal of Biochemistry), 270: 4762-4770***

29. R. Pagani, M. Song, M. McEnery, **N. Qin**, R. W. Tsien, L. Toro, E. Stefani and O. D. Uchitel (2004) "Differential expression of alpha 1 and beta subunits of voltage dependent Ca^{2+} channel at the neuromuscular junction of normal and P/Q Ca^{2+} channel knockout mouse". ***Neuroscience: 123 (1)***: 75-85

30. **N. Qin**, SP Zhang,, T.L. Reitz, J.M. Mei and C.M. Flores (2005) "Cloning, Expression and Functional Characterization of Human COX-1 Splicing Variants: Evidence for Intron 1 Retention" ***The Journal of Pharmacology and Experimental Therapeutics, 315 (3): 1298-1305***

31. Y. Liu, M. Lubin, T.L. Reitz, Y. Wang, R.W. Colburn, C.M. Flores and **N. Qin** (2006) "Molecular identification and functional characterization of a temperature-sensitive transient receptor potential channel (TRPM8) from canine" ***European Journal of Pharmacology, 530: 23-32***

32. Y. Liu, **N. Qin,** T.L. Reitz, Y. Wang and C.M. Flores (2006) "Inhibition of the rat brain sodium channel Nav1.2 after prolonged exposure to gabapentin" ***Epilepsy Research 69 (3):***

Book Chapters

1. L. Birnbaumer, **N. Qin**, R. Olcese, E. Tareilus and E. Stefani, (1998). "Studies on the regulation of the human neuronal calcium channel by β and $\alpha_2\delta$ subunits". ***Low voltage activated T-type calcium channels***, 258-268, Montpellier, France

2. F. Noceti, R. Olcese, P. Baldelli, **N. Qin,** L. Birnbaumer and E. Stefani, (1998) "Charges per channel in Ca^{2+} channels: effect of the regulatory β subunit co-expression on α_1 pore forming subunit". ***Low voltage activated T-type calcium channels***, 307-313, Montpellier, France

3. R. Olcese, F. Noceti, P. Baldelli, **N. Qin,** L. Birnbaumer and E. Stefani, (1998) "β subunit modulation of the coupling between charge movement and pore opening in calcium channels". ***From Ion Channels to Cell to Cell Conversation***, 91-104, Plenum press, New York and London

4. L. Birnbaumer, **N. Qin**, R. Olcese, E. Tareilus, Daniela Platano and E. Stefani, (1998) Structures and Functions of Calcium Channel β Subunits." ***J. of Bioenergetics and Biomembranes,*** Vol. 30(4) 357-375

5. L. Birnbaumer, G. Boulay, D. Brown, M. Jiang, A. Doetrich, K Mikoshiba, X. Zhu, and **N. Qin**, (2000) "Mechanism of Capacitative Ca^{2+} entry (CCE): Interaction between IP3 Receptor and TRP links the Internal Calcium Storage Compartment to Plasma Membrane CCE Channels." ***Recent Progress in Hormone Research, Vol. 55:*** 127-162

ABSTRACTS

1. Y. Liu, M.L. Lubin, T. Reitz, R.W. Colburn, C.M. Flores, and **N. Qin** "Cloning and functional characterization of a canine transient receptor potential channel, cTRPM8". 2004 Neuroscience Meeting
2. **N. Qin**, S-P. Zhang, T. Reitz, E. E. Codd and C. M. Flores "Human COX-3? Cloning and Characterization of a splicing variant of COX-1" 2004 Neuroscience meeting
3. **N. Qin,** M. Neeper, Y. Liu and C. M. Flores "Characterization of calcium channel beta subunit interaction domain" 2005 International Association for the Study of Pain Annual Meeting

PATENTS

1. **N. Qin,** E. Codd, and M. D'Andrea (2006) "The Human Voltage Gated Sodium Channel β_{1A} Subunit And Method Of Use." ***US 6994,993 B2***
2. **N. Qin** and E. Codd (2003) "cDNA encoding the human alpha2delta-4 calcium channel subunit" US20030166045 A1
3. **N. Qin**, E. Codd C. M. Flores and SP. Zhang (2004) "Human cyclooxygenase-3 enzyme and uses thereof" US20040235017 A1
4. C. M. Flores, Y. Liu, M. Lubin and **N. Qin** (2006) "Canine Cold- And Menthol-Sensitive Receptor 1" ***US20060014246 A1***
5. **N. Qin**, Y. Liu, M. Neeper, T. Reitz and C. M. Flores (2005) "Compositions and Methods for Identifying Modulators of TRPV2" Provisional filing
6. **N. Qin**, Y. Liu and C. M. Flores (2005) "A Polypeptide Complex of TRPM8 and Calmodulin And Its Uses Thereof" Provisional filing

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No. 15798- 1

Project No. α2δ of cat channel Protocol / Experiment No. ..... Date 9/20/99

Subject ..... Purpose cloning

Contd. from page _____

Search Genebank for all published Calcium channels
916 documents

NCBI Entrez **Nucleotide QUERY** BLAST Entrez ?

Current Query

Details **Search** : calcium channel[All Fields] --> Retrieve 916 Documents

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Search Field: All Fields Search Mode: Automatic

Enter Terms: Search Clear

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Clear All

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Term (Total Records)

calcium channel[All Fields] (916)

Search for the Intersection (AND) of the selected terms.

Questions or comments? Write to the NCBI Help Desk.

Contd. on page _____ Investigator Alias Qin Date 9/28/99

Read and Understood Ellen Todd Date 10/7/99

No. 15798- 6

Project No. $\alpha_2 8$ Protocol / Experiment No. ..... Date 9/28/99

Subject ..... Purpose .....

Contd. from page 5

Analysis and Comparison of other small fragments of $\alpha_2 8$ identified on 9/20/99.

Two fragments are named $\alpha_2 8$.
name them to $\alpha_2 8$-4.

they are H86016.
g1436938.

Two are human $\alpha_2 8$-3 fragments.
they are g3805345
g2885043. or AA001473

sequence comparison result of H86016
& S1436938

are saved in
H:/mydata/seqe/$\alpha_2 8$/new-a2d.

Contd. on page 7 Investigator [signature] Date 10/1/99

Read and Understood E Todd Date 100799

No. 15798- 8

Project No. $\alpha_2\delta$. Protocol / Experiment No. Date 9/30/99

Subject Purpose

Contd. from page 7

1. comparison of 208672.2
19 9408.3
w. 66 mouse $\alpha_2\delta$-3.
same as H:/mydata/gene/a2d/Inayte clone 208672
Inayte clone 199408.

2. Design oligos.

A2-3-5
-6
-7
-8
-9
-10
} for clone human $\alpha_2\delta$-3.

A2-4-1
-2
-3
-4
-5
} for clone human $\alpha_2\delta$-4

Contd. on page 6 Investigator [signature] Date 10/1/99

Read and Understood E Cold Date 100799

Project No. $\alpha_2\delta$ & Na-βIA Protocol / Experiment No. Date 10-2-99

Subject Purpose

Contd. from page

1. Race PCR to amplify NT of hα2δ-4.
Marathon Ready library ① fetal human brain
② human brain.

RX. 5ul 10x Buffer.
5ul cDNA library.
1ul API.
1ul Ax-4-9 (10 pmol/ul).
1ul Advantage Taq.
1ul 10mM dNTP.
36ul H_2O

cycles. 94°C/30"
↓
94°C/5" ↖ 5 cycles.
↓
72°C/4min
↓
94°C/5" ↖ 5 cycles.
↓
70°C/4min
↓
94°C/5" ↖ 25 cycles.
↓
68°C/4 min
↓
4°C/parking.

Contd. on page 22 Investigator Date 11/16/99

Read and Understood Date 3-6-00

No. 15798- 28

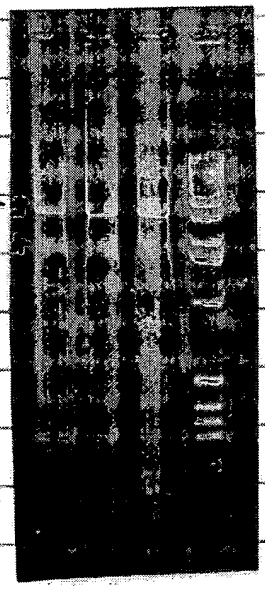
Project No. α2δ+ Na-βIA Protocol / Experiment No. ..... Date 11-89

Subject ..... Purpose .....

Contd. from page _____

1. cloning Race PCR product (11-5-99) of NT α2δ-4 (human)

① gel purification
cut two parts.
A. 3Kb band
B 2-2.5 Kb bands
purify them
separately



② ptrich them.
③ Ligation pBcript.
④ transform to XL10-gold

2. Retest condition for Na-βIA.
RX 50 ul. with Advantage Taq

① SB1-4 + SB1-2. } rat brain cDNA
② SB1-5 + SB1-2 }
③ SB1-1 + SB1-2 } human brain cDNA
④ SB1-5 + SB1-2 }

condition: 30 cycle.
94°C/30" → [58°C/30"] → 72°C/60"

Sul to check PCR RX.
does not work

Contd. on page 75 Investigator _____ Date 11/16/99

Read and Understood _____ Date 3-6-00

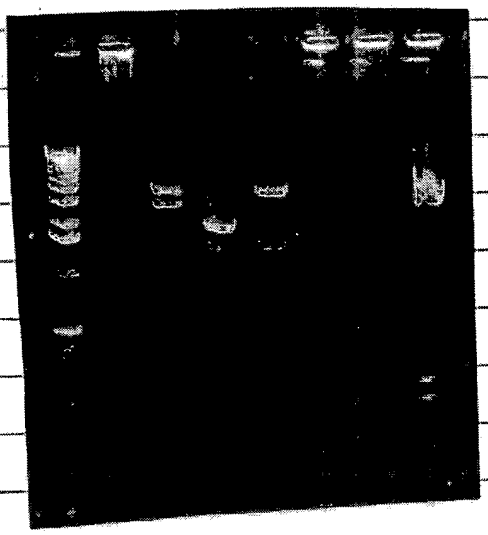
Project No. α2 8. Protocol / Experiment No. ..... Date 11-11-99

Subject ..... Purpose .....

Contd. from page _____

1. miniprep BQC44.
two new 3Kb α2 8-4 in pCR2.1
four new 2kb α2 8-4 in pCR2.1
dig. NQC44 with EcoRI + NotI
all others with EcoRI only

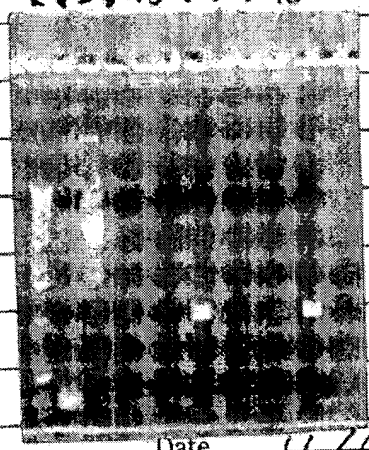
3-1 3-2 2-1 2-2 2-3 2-4 NQC44.



3-2, 2-1, & 2-2
have insertion
3-2 → NQC45
2-1 → NQC46
2-2 → NQC47

Send NQc44-47
for seq.

2. characterise these clones. by PCR. TTHA2-4-2 Rm+Rv2-4-2
① NQC44, ② NQC45, ③ NQC46
④ NQ47, ⑤ Insyte 3343341
20 ul RX.
NQC44 & 45 are very promising
but 44 is too short.
45 is right size.



Contd. on page 32 Investigator _____ Date 11/16/99

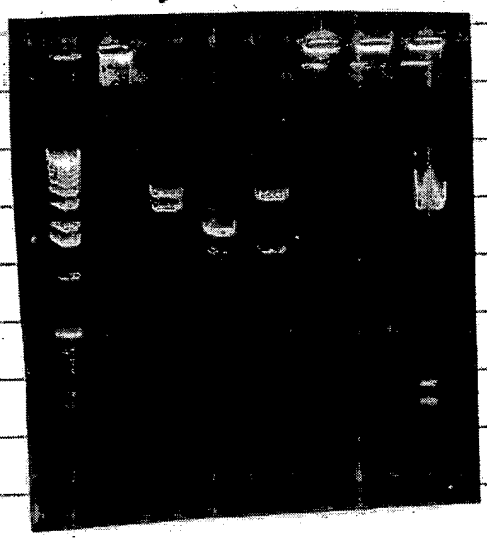
Read and Understood _____ Date 3-6-00

Project No. 028 Protocol / Experiment No. Date 11-11-99

Subject Purpose

Contd. from page

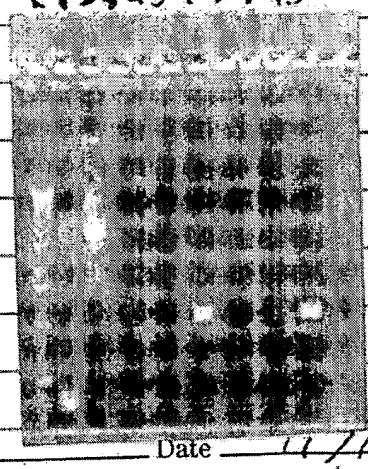
1. miniprep BQC44.
two new 3kb 028-4 in pCR2.1
four new 2kb 028-4 in pCR2.1
dig. NQC44 with EcoRI + NotI
all others with EcoRI only
3-1 3-2 2-1 2-2 2-3 2-4, NQC44.



3-2, 2-1, & 2-2
have insertion
3-2 → NQC45
2-1 → NQC46
2-2 → NQC47

Send NQC44-47
for seq.

2. characterise these clones. by PCR. T7+A2-4-2 RV+A2-4-2
① NQC44, ② NQC45, ③ NQC46
④ NQ447, ⑤ negte 3343341
1 2 3 4 5 1 2 3 4 5
20 ml RX.
NQC44 & 45 are very promising
but 44 is too short.
45 is right size.



Contd. on page 32 Investigator Date 11/16/99

Read and Understood N/W Date 3-6-00

Project No. αvβ / Cα-α2δ Protocol / Experiment No. ..... Date 4/7/00

Subject ..... Purpose .....

Contd. from page _____

2. Analysis of Data of hα2δ-4 NT.
They (NQC190-195) are all hα2δ-4 NT.
finished clones of α2δ-4.

Syn #1.300: A2-4-27 } for added HA on hα2δ-4 CT
A2-4-28

A2-3-29 } added HA on
A2-3-30 } hα2δ-3 CT

 Investigator _____ Date 4/14/00

Read and Understood _____ Date 4/21/00

ha2d-4b.pep

Text View

```
!!AA_SEQUENCE 1.0

ha2d-4.pep  Length: 1090  April 7, 2000 14:19  Type: P  Check: 9269  ..

       1  MAVALGTRRR DRVKLWADTF GGDLYNTVTK YSGSLLLQKK YKDVESSLKI

      51  EEVDGLELVR KFSEDMENML RRKVEAVQNL VEAAEEADLN HEFNESLVFD

     101  YYNSVLINER DEKGNFVELG AEFLLESNAH FSNLPVNTSI SSVQLPTNVY

     151  NKDPDILNGV YMSEALNAVF VENFQRDPTL TWQYFGSATG FFRIYPGIKW

     201  TPDENGVITF DCRNRGWYIQ AATSPKDIVI LVDVSGSMKG LRMTIAKHTI

     251  TTILDTLGEN DFVNIIAYND YVHYIEPCFK GILVQADRDN REHFKLLVEE

     301  LMVKGVGVVD QALREAFQIL KQFQEAKQGS LCNQAIMLIS DGAVEDYEPV

     351  FEKYNWPDCK VRVFTYLIGR EVSFADRMKW IACNNKGYYT QISTLADTQE

     401  NVMEYLHVLS RPMVINHDHD IIWTEAYMDS KLLSSQAQSL TLLTTVAMPV

     451  FSKKNETRSH GILLGVVGSD VALRELMKLA PRYKLGVHGY AFLNTNNGYI

     501  LSHPDLRPLY REGKKLKPKP NYNSVDLSEV EWEDQAESLR TAMINRETGT

     551  LSMDVKVPMD KGKRVLFLTN DYFFTDISDT PFSLGAVLSR GHGEYILLGN

     601  TSVEEGLHDL LHPDLALAGD WIYCITDIDP DHRKLSQLEA MIRFLTRKDP

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Human $\alpha_2\delta$-4 map

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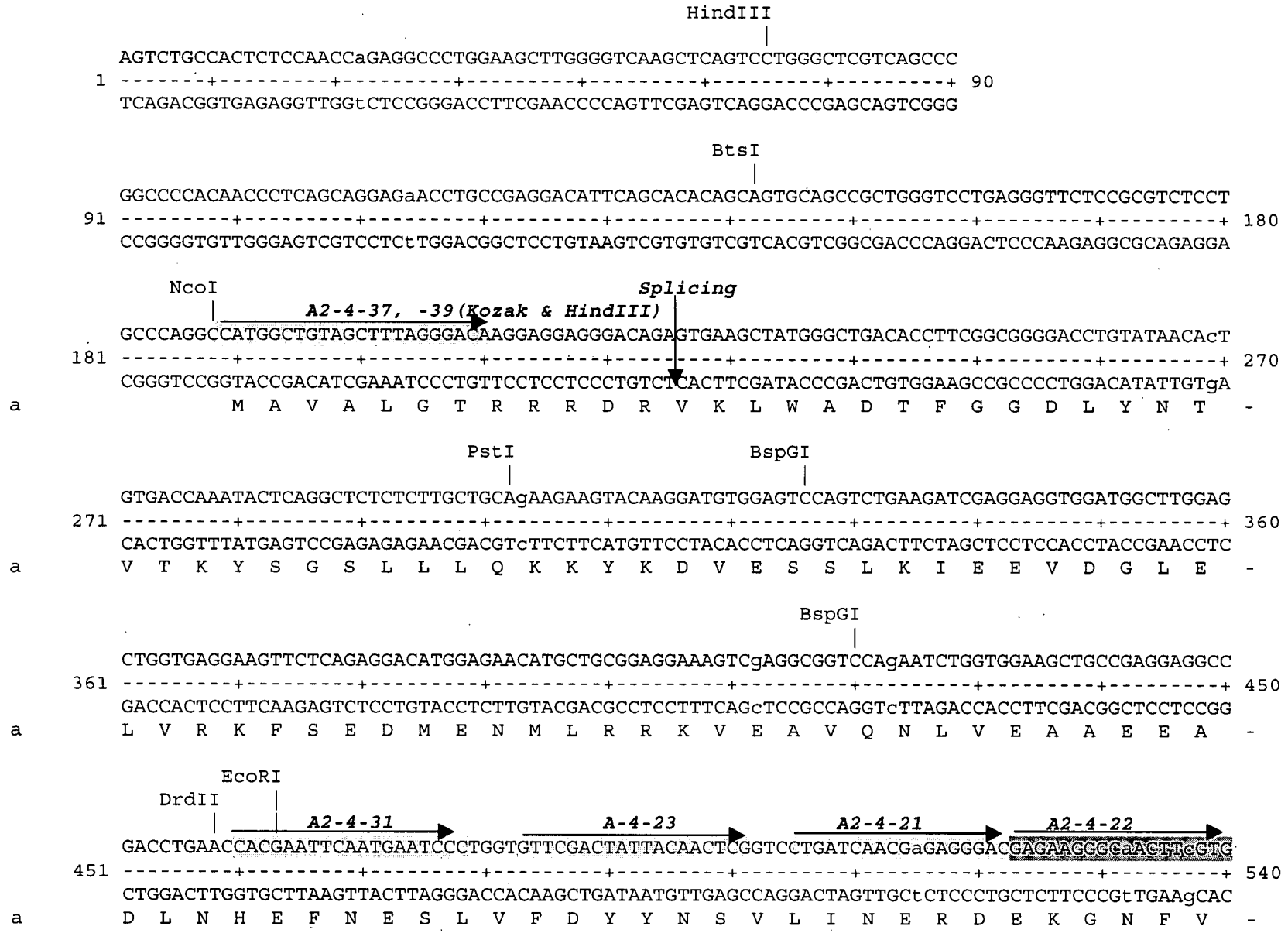

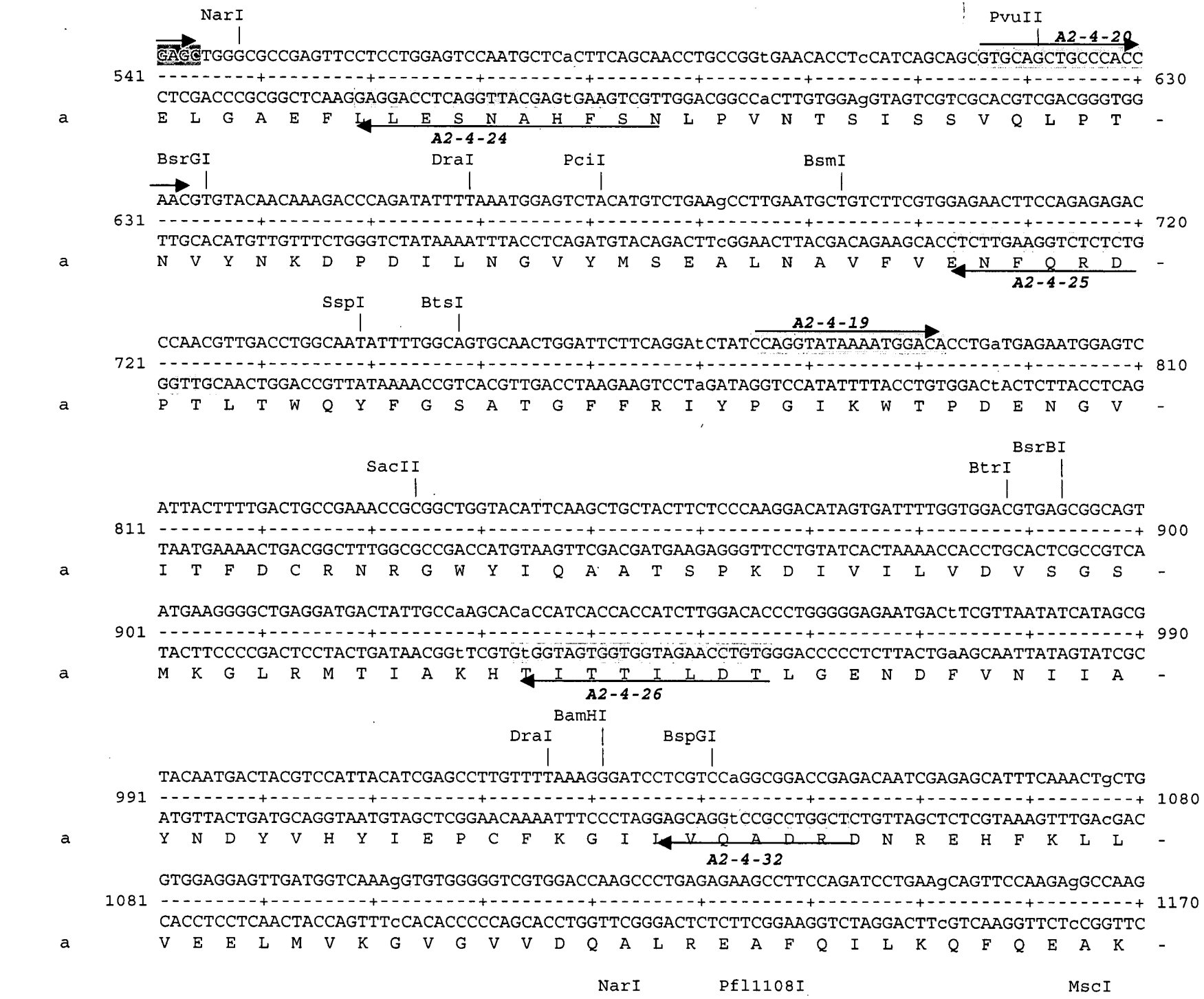
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SacII
BtrI
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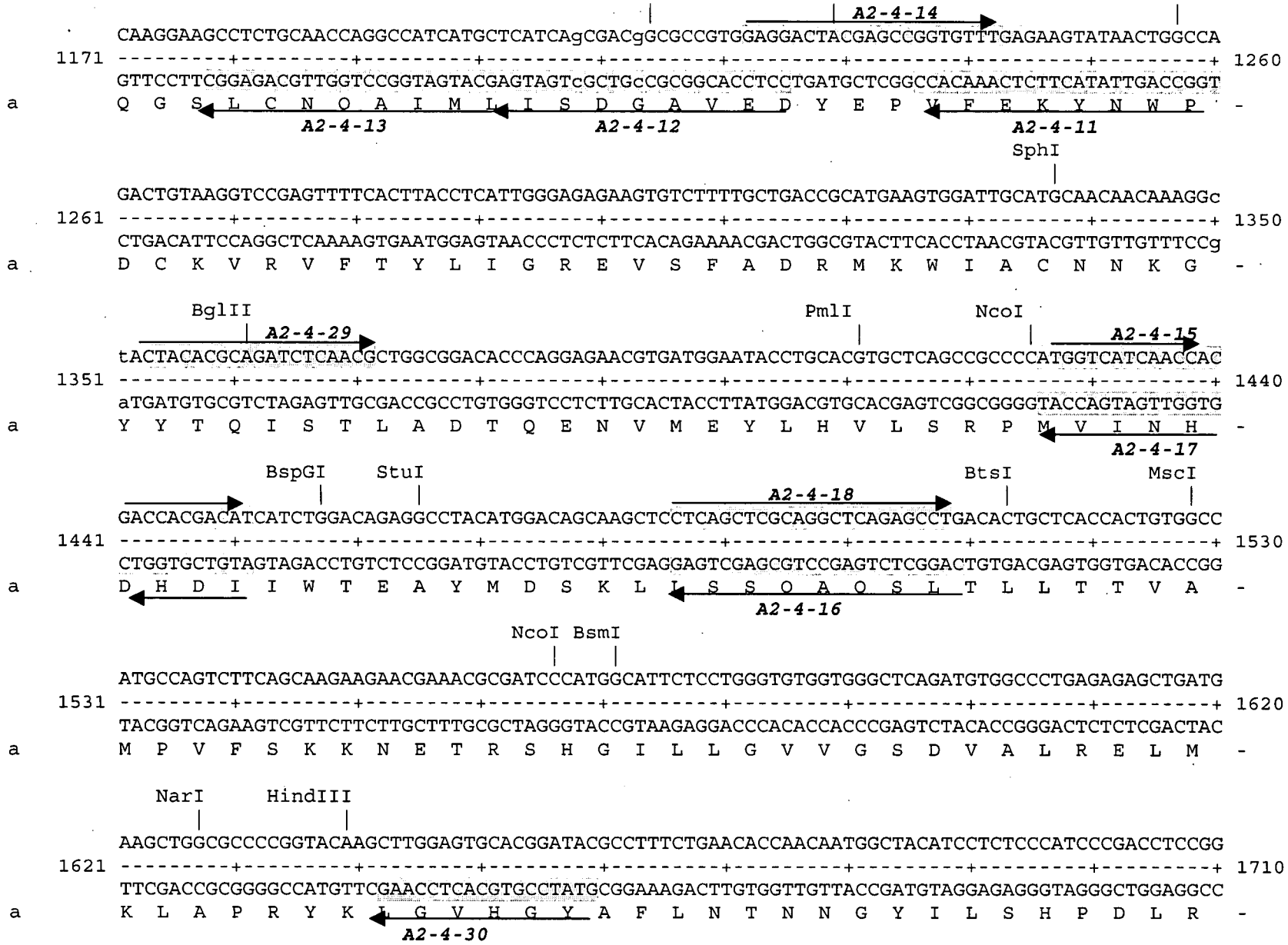
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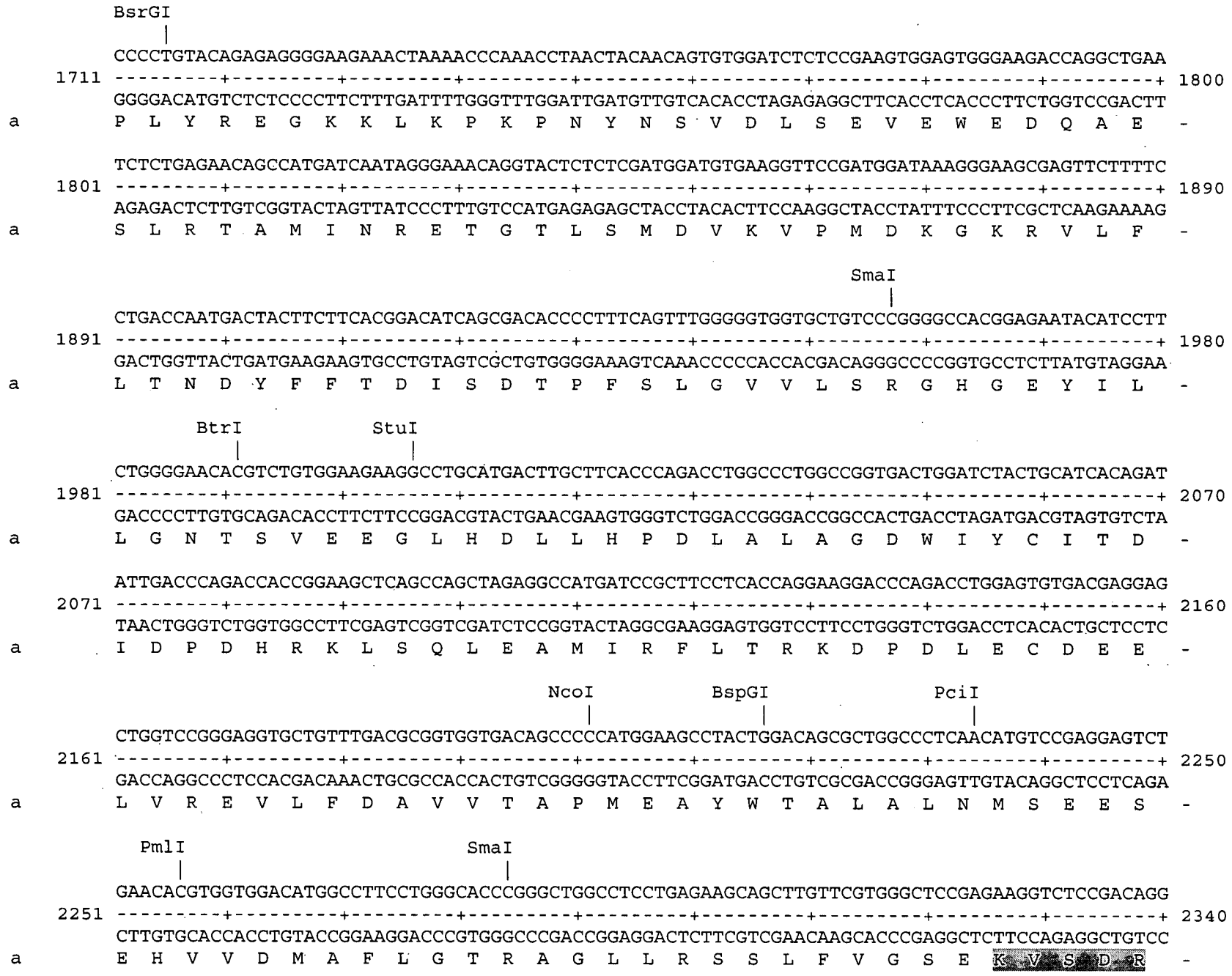
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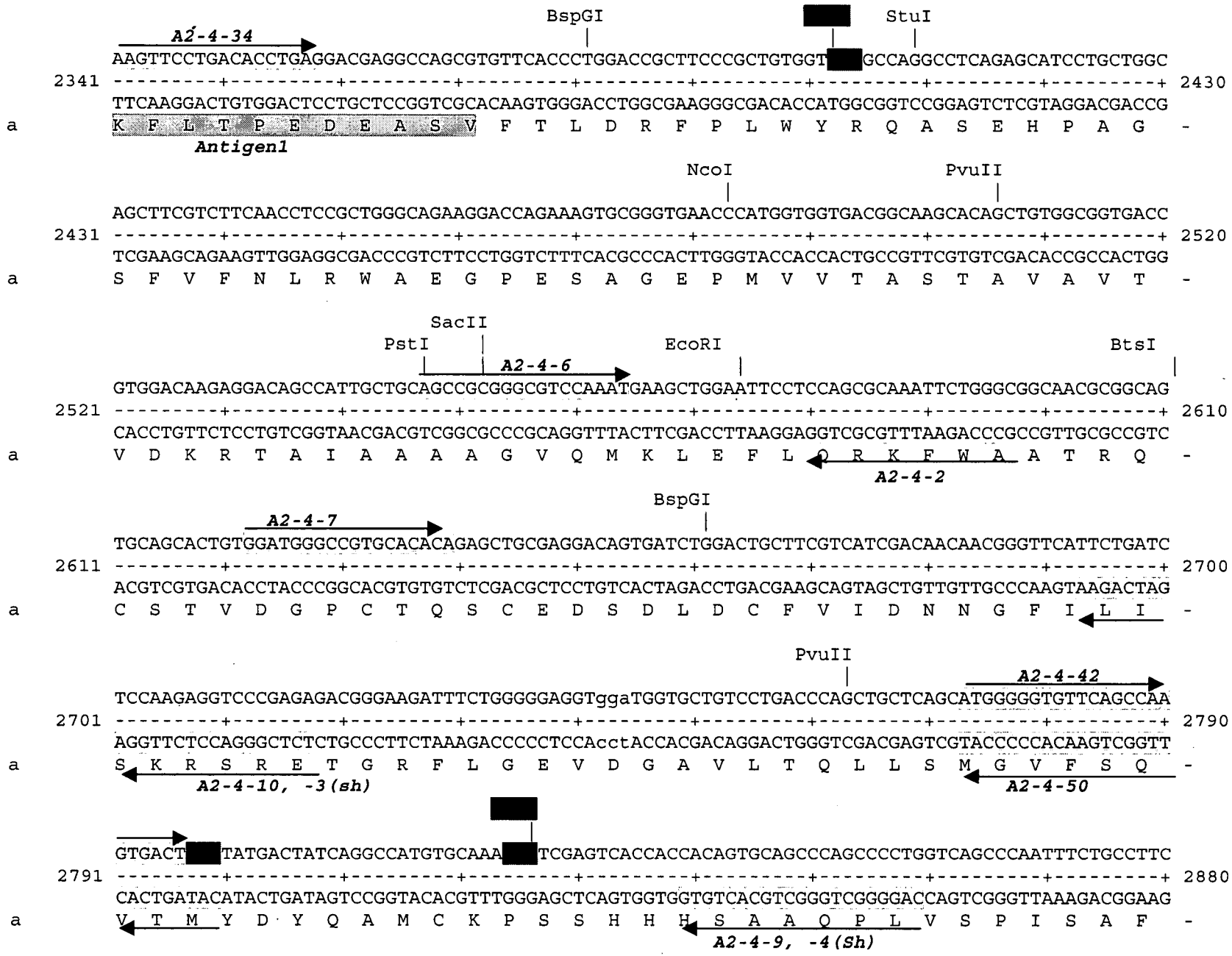
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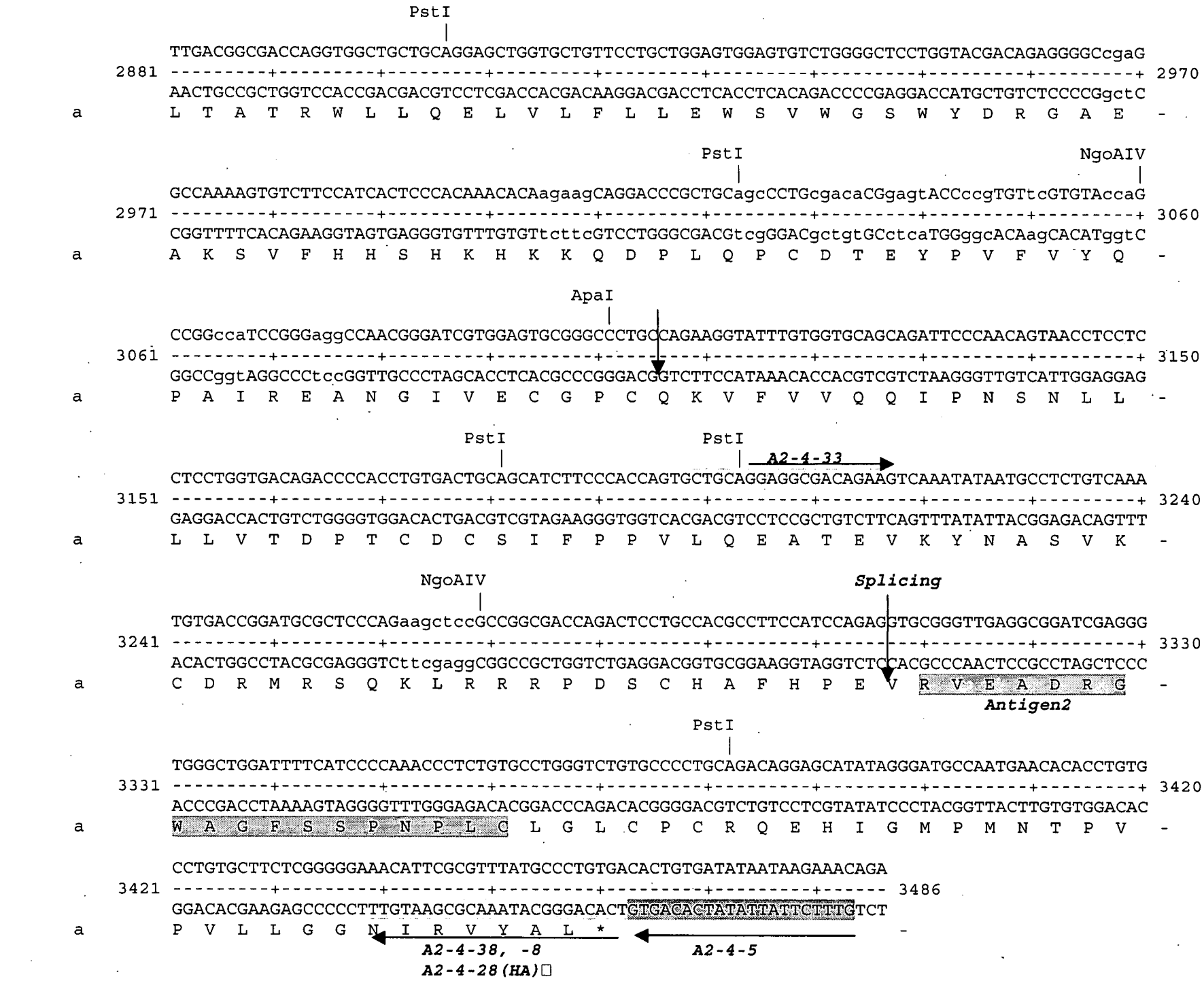
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A2-4-38, -8
A2-4-28(HA)
A2-4-5

Enzymes that do cut and were not excluded:

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HindIII	KpnI	MscI	NarI	NcoI	NgoAIV	PciI	Pfl1108I	PmlI	PstI	PvuII	SacII
SmaI	SphI	SspI	StuI	XhoI							

Enzymes that do not cut:

BsbI	BssHII	BssSI	BstZ17I	ClaI	EagI	EcoRV	HpaI	Kpn2I	MluI	MunI	NdeI
NheI	NotI	NruI	NsiI	NspV	PacI	PinAI	PsiI	PvuI	RcaI	SacI	SalI
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V  T  K  Y  S  G  S  L  L  L  Q  K  K  Y  K  D  V  E  S  S  L  K  I  E  E  V  D  G  L  E
L  V  R  K  F  S  E  D  M  E  N  M  L  R  R  K  V  E  A  V  Q  N  L  V  E  A  A  E  E  A
D  L  N  H  E  F  N  E  S  L  V  F  D  Y  Y  N  S  V  L  I  N  E  R  D  E  K  G  N  F  V
E  L  G  A  E  F  L  L  E  S  N  A  H  F  S  N  L  P  V  N  T  S  I  S  S  V  Q  L  P  T
N  V  Y  N  K  D  P  D  I  L  N  G  V  Y  M  S  E  A  L  N  A  V  F  V  E  N  F  Q  R  D
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I  T  F  D  C  R  N  R  G  W  Y  I  Q  A  A  T  S  P  K  D  I  V  I  L  V  D  V  S  G  S
M  K  G  L  R  M  T  I  A  K  H  T  I  T  T  I  L  D  T  L  G  E  N  D  F  V  N  I  I  A
Y  N  D  Y  V  H  Y  I  E  P  C  F  K  G  I  L  V  Q  A  D  R  D  N  R  E  H  F  K  L  L
V  E  E  L  M  V  K  G  V  G  V  V  D  Q  A  L  R  E  A  F  Q  I  L  K  Q  F  Q  E  A  K
Q  G  S  L  C  N  Q  A  I  M  L  I  S  D  G  A  V  E  D  Y  E  P  V  F  E  K  Y  N  W  P
D  C  K  V  R  V  F  T  Y  L  I  G  R  E  V  S  F  A  D  R  M  K  W  I  A  C  N  N  K  G
Y  Y  T  Q  I  S  T  L  A  D  T  Q  E  N  V  M  E  Y  L  H  V  L  S  R  P  M  V  I  N  H
D  H  D  I  I  W  T  E  A  Y  M  D  S  K  L  L  S  S  Q  A  Q  S  L  T  L  L  T  T  V  A
M  P  V  F  S  K  K  N  E  T  R  S  H  G  I  L  L  G  V  V  G  S  D  V  A  L  R  E  L  M
K  L  A  P  R  Y  K  L  G  V  H  G  Y  A  F  L  N  T  N  N  G  Y  I  L  S  H  P  D  L  R
P  L  Y  R  E  G  K  K  L  K  P  K  P  N  Y  N  S  V  D  L  S  E  V  E  W  E  D  Q  A  E
S  L  R  T  A  M  I  N  R  E  T  G  T  L  S  M  D  V  K  V  P  M  D  K  G  K  R  V  L  F
L  T  N  D  Y  F  F  T  D  I  S  D  T  P  F  S  L  G  A  V  L  S  R  G  H  G  E  Y  I  L
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E  H  V  V  D  M  A  F  L  G  T  R  A  G  L  L  R  S  S  L  F  V  G  S  E  K  V  S  D  R
K  F  L  T  P  E  D  E  A  S  V  F  T  L  D  R  F  P  L  W  Y  R  Q  A  S  E  H  P  A  G
S  F  V  F  N  L  R  W  A  E  G  P  E  S  A  G  E  P  M  V  V  T  A  S  T  A  V  A  V  T
V  D  K  R  T  A  I  A  A  A  A  G  V  Q  M  K  L  E  F  L  Q  R  K  F  W  A  A  T  R  Q
C  S  T  V  D  G  P  Y  T  Q  S  C  E  D  S  D  L  D  C  F  V  I  D  N  N  G  F  I  L  I
S  K  R  S  R  E  T  G  R  F  L  G  E  V  D  G  A  V  L  T  Q  L  L  S  M  G  V  F  S  Q
V  T  M  Y  D  Y  Q  A  M  C  K  P  S  S  H  H  H  S  A  A  Q  P  L  V  S  P  I  S  A  F
L  T  A  T  R  W  L  L  Q  E  L  V  L  F  L  L  E  W  S  V  W  G  S  W  Y  D  R  G  A  E
A  K  S  V  F  H  H  S  H  K  H  K  K  Q  D  P  L  Q  P  C  D  T  E  Y  P  V  F  V  Y  Q
P  A  I  R  E  A  N  G  I  V  E  C  G  P  C  Q  K  V  F  V  V  Q  Q  I  P  N  S  N  L  L
L  L  V  T  D  P  T  C  D  C  S  I  F  P  P  V  L  Q  E  A  T  E  V  K  Y  N  A  S  V  K
C  D  R  M  R  S  Q  K  L  R  R  R  P  D  S  C  H  A  F  H  P  E  V  R  V  E  A  D  R  G
W  A  G  F  S  S  P  N  P  L  C  L  G  L  C  P  C  R  Q  E  H  I  G  M  P  M  N  T  P  V
P  V  L  L  G  G  N  I  R  V  Y  A  L
```

Comparison of hα2δ-4.pep with hα2δ-3.pep:

April 7, 2000 14:19

Percent Similarity: 69.172 Percent Identity: 60.133

```
                .         .         .         .         .
 1 ....................MAVALGTRRRDR.......VKLWADTFG 21
                       :  |||   |         |||||  ||
 1 MAGPGSPRRASRGASALLAAALLYAALGDVVRSEQQIPLSVVKLWASAFG 50
                .         .         .         .         .
22 GDLYNTVTKYSGSLLLQKKYKDVESSLKIEEVDGLELVRKFSEDMENMLR 71
   |:: .   ||||| |||||||: |  . |||:|||:||:| ...|| |
51 GEIKSIAAKYSGSQLLQKKYKEYEKDVAIEEIDGLQLVKKLAKNMEEMFH 100
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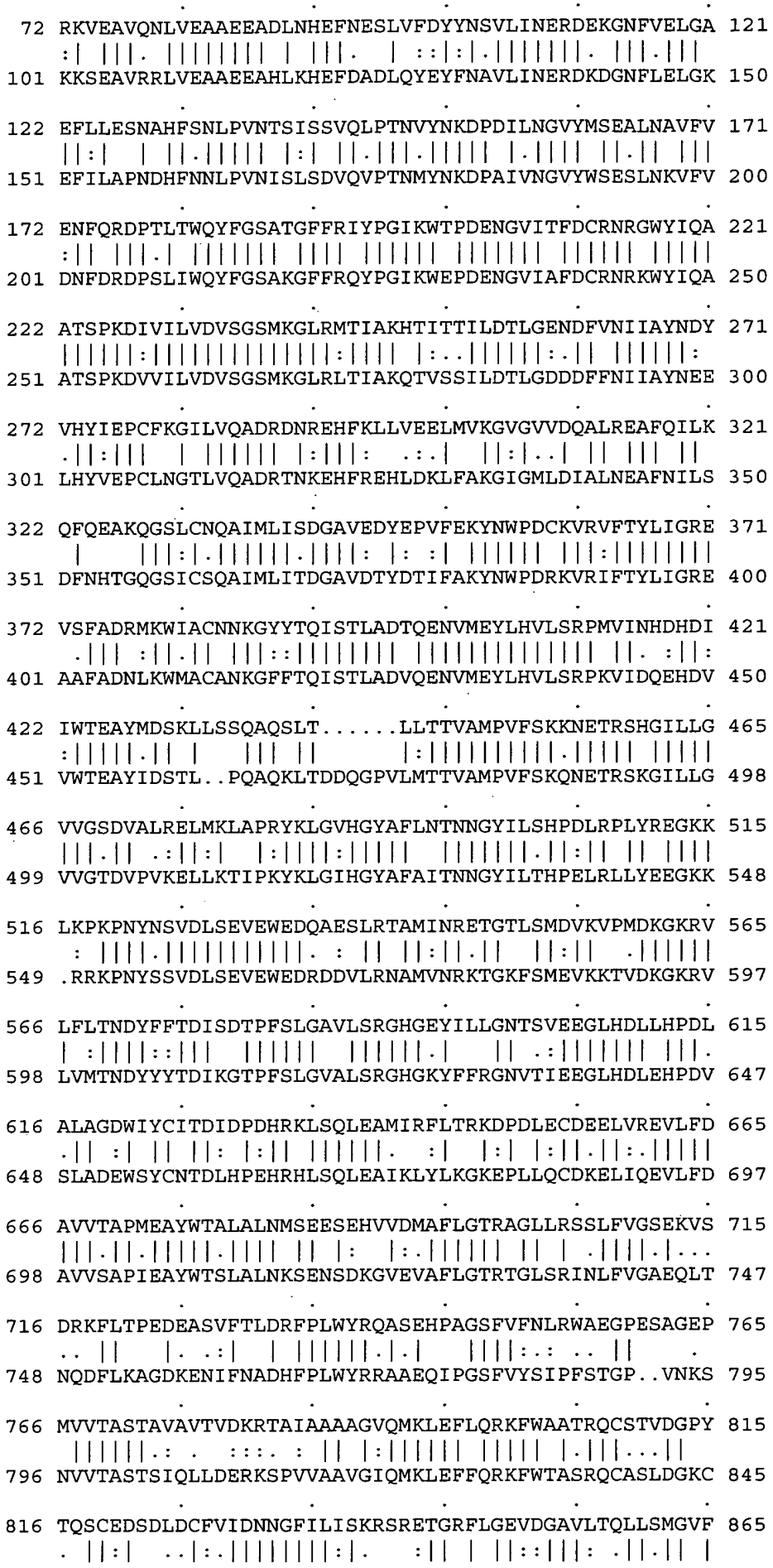

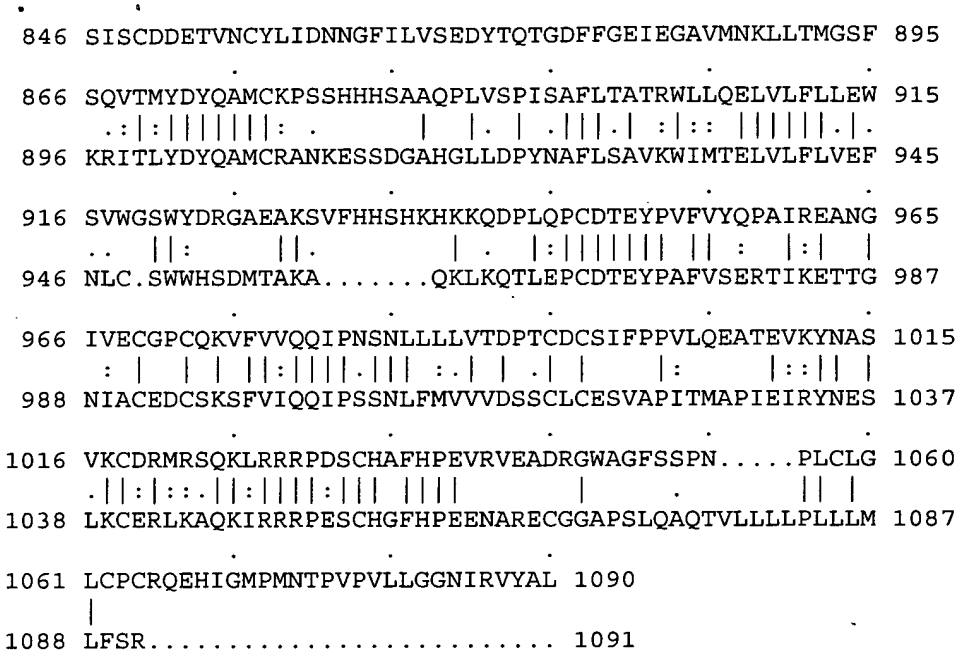
846 SISCDDETVNCYLIDNNGFILVSEDYTQTGDFFGEIEGAVMNKLLTMGSF 895
866 SQVTMYDYQAMCKPSSHHHSAAQPLVSPISAFLTATRWLLQELVLFLLEW 915
896 KRITLYDYQAMCRANKESSDGAHGLLDPYNAFLSAVKWIMTELVLFLVEF 945
916 SVWGSWYDRGAEAKSVFHHSHKHKKQDPLQPCDTEYPVFVYQPAIREANG 965
946 NLC.SWWHSDMTAKA.......QKLKQTLEPCDTEYPAFVSERTIKETTG 987
966 IVECGPCQKVFVVQQIPNSNLLLLVTDPTCDCSIFPPVLQEATEVKYNAS 1015
988 NIACEDCSKSFVIQQIPSSNLFMVVVDSSCLCESVAPITMAPIEIRYNES 1037
1016 VKCDRMRSQKLRRRPDSCHAFHPEVRVEADRGWAGFSSPN.....PLCLG 1060
1038 LKCERLKAQKIRRRPESCHGFHPEENARECGGAPSLQAQTVLLLLPLLLM 1087
1061 LCPCRQEHIGMPMNTPVPVLLGGNIRVYAL 1090
1088 LFSR..... 1091